Lebrikizumab Demonstrates Progressive Improvements in Skin Clearance and Itch Relief Over One Year in Patients With Atopic Dermatitis

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BACKGROUND

- AD is a chronic skin disease associated with serious burden, affecting sleep, daily activities, and social relationships[1]
- Lebrikizumab is a monoclonal antibody that binds with high affinity and slow off-rate to IL-13, thereby blocking the downstream effects of IL-13 with high potency[2]
- Lebrikizumab has demonstrated efficacy and positive benefit-risk profile as monotherapy for moderate-to-severe AD at the 16-week primary endpoints of the 2 Phase 3, randomized, double-blind, placebo-controlled, 52-week ADvocate1 (NCT04146363) and ADvocate2 (NCT04178967) trials[3,4]
  - Due to re-randomization at Week 16, the design of these studies does not allow for a continuous view of patients' response trajectory from Weeks 0 to 52

Note: Statistical results of the primary and major secondary endpoints for ADvocate1 and ADvocate2 were confirmed through replicate statistical programming, validation, and quality reviews[3,4]

OBJECTIVE

- To estimate the response trajectory for patients continuously treated with lebrikizumab from baseline to Week 52
  - This analysis was designed to mimic lebrikizumab treatment as it may appear in the real-world, under the assumption that Intent-to-Treat patients received lebrikizumab Q2W treatment for the first 16 weeks, then received lebrikizumab Q4W if they responded[a] to initial lebrikizumab treatment, or continued to receive Q2W treatment if they did not respond

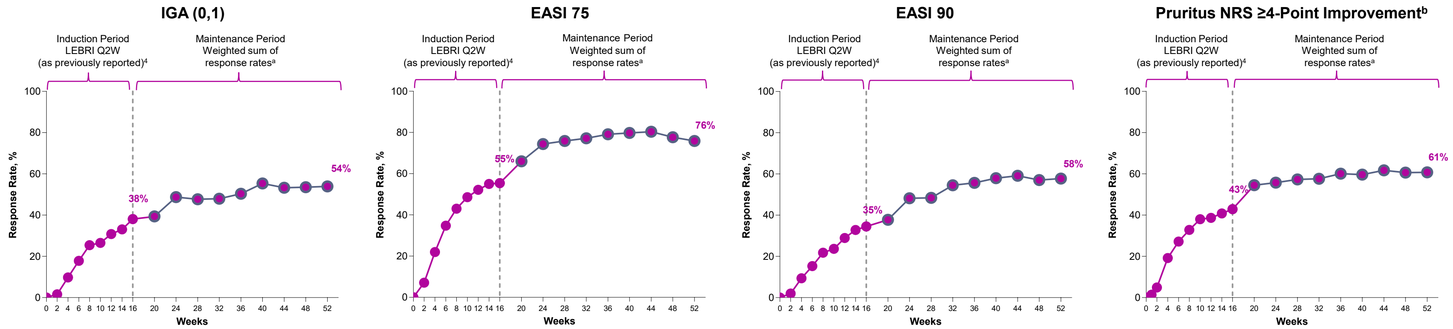
[a] Responders achieved IGA (0,1) with ≥2-point improvement or EASI 75 from baseline to Week 16 without rescue medication

CONCLUSIONS

- Based on this model, treatment with lebrikizumab resulted in continuous and progressive skin and itch improvements from Weeks 0 to 52
- As these trials were not designed as treat-through, these results should be interpreted with caution

SUMMARY OF KEY FINDINGS

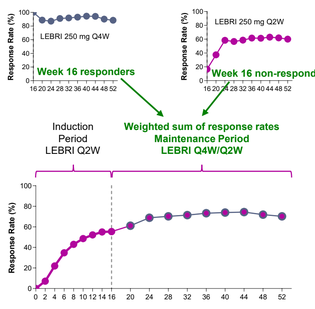
Treat-Through Model: Calculated Continuous Improvement From Baseline Through Week 52



[a] MPP LEBRI Q4W arm and unblinded MEP LEBRI Q2W arm response rates; [b] In patients with ≥4-point Pruritus NRS at baseline

METHODS

Treat-Through Model



Note: Responders were defined as having an IGA (0,1) with ≥2-point improvement or achieving EASI 75 from baseline to Week 16, without receiving topical or systemic rescue medication

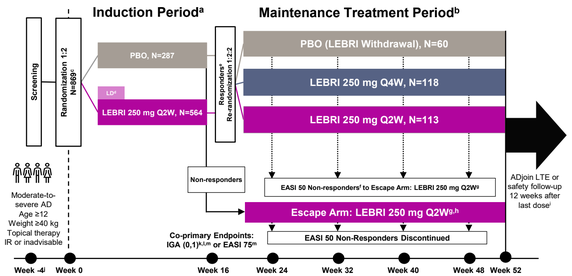
Statistical Analysis

- The Induction Period analysis was based on the pooled ADvocate 1&2 mITT population assigned to lebrikizumab Q2W at baseline
- The estimate of the response rates from Week 16 to Week 52 is based on a weighted sum of the response rates from 2 treatment arms at each time point:
  - Responders[a] at Week 16 who received blinded lebrikizumab Q4W treatment during the 36-week Maintenance Period (MPP)
  - Patients who did not meet per-protocol response criteria[a] at Week 16 continued lebrikizumab Q2W as unblinded treatment in the Escape Arm for the 36-week Maintenance Period (MEP)
  - The weights assigned to the 2 treatment arms are the proportion of lebrikizumab-treated mITT patients who were re-randomized to blinded treatment, or entered the Escape Arm, respectively
- Data after treatment discontinuation due to lack of efficacy were imputed with NRI; data after treatment discontinuation due to other reasons and other missing data were imputed with MI, throughout the 52-week treatment
  - In the Induction Period, patients who used rescue medication were considered non-responders; data collected after use of rescue medication (topical or systemic) were imputed using NRI
  - In the Maintenance Period, use of intermittent topical rescue medications was permitted; observed data after rescue medication use were included
  - Patients in the Maintenance Blinded Treatment Arm not maintaining EASI 50 during the Maintenance Period were discontinued from the assigned blinded treatment (eligible for Escape Arm)
  - Patients in the Escape Arm not achieving or maintaining an EASI 50 score after 8 weeks of treatment were terminated from the trial

[a] Responders were defined as having an IGA (0,1) with ≥2-point improvement or achieving EASI 75 from baseline to Week 16, without receiving topical or systemic rescue medication

Study Design

ADvocate1 and ADvocate2



[a] Use of topical/systemic treatments for AD prohibited; [b] Use of intermittent topical rescue medications for AD permitted. Responders who received PBO during induction who were re-randomized to LEBRI received an LD of either 500 mg given at W16 or 500 mg given at W16 and W18; [c] 424 patients (ADvocate1) and 445 patients (ADvocate2) with moderate-to-severe AD; [d] 500 mg LD at W0 and W2; [e] Responders achieved EASI 75 or IGA (0,1) with ≥2-point improvement at W16 without rescue medication use; [f] Patients who did not maintain ≥EASI 50 were assigned to the Escape Arm; [g] Maintenance of response assessed by EASI 50 at W24, W32, W40, and W48, respectively. Patients who received systemic rescue medication were required to washout for 5 half-lives prior to initiating treatment in the Escape Arm; [h] Participants who were eligible for the Escape Arm at W16 received blinded LD at W16 and W18, based on their prior treatment assignment; [i] Patients completing ADvocate1/2 were offered open-label treatment in ADjoin, otherwise patients participated in a safety follow-up 12 weeks after their last dose; [j] ≤30-day screening period; [k] IGA (0,1) with ≥2-point improvement from baseline; [l] FDA primary endpoint; [m] EMA co-primary endpoint

Outcomes

- IGA (0,1) response of clear or almost clear
- EASI 75 response
- EASI 90 response
- Pruritus NRS ≥4-point improvement from baseline:
  - Pruritus NRS is a patient-reported, single-item, daily, 11-point scale, which assesses itch from 0 "no itch" to 10 "worst itch imaginable"[5]
  - The baseline mean was the average of the daily scores in the week prior to the first injection
  - Post-baseline weekly scores were calculated by averaging the daily scores from the previous 7 days for patients with ≥1 non-missing values
  - Assessed in patients with ≥4-point Pruritus NRS at baseline

Key Eligibility Criteria

- Adults or adolescents (≥12 to <18 years of age; weight ≥40 kg)
- Diagnosis of AD, as defined by the American Academy of Dermatology Consensus Criteria, for ≥1 year before screening
- Moderate-to-severe AD, defined as having all the following at the baseline visit:
  - EASI ≥16
  - IGA ≥3
  - BSA involvement ≥10%
- Candidate for systemic therapy

RESULTS

Baseline Demographics and Disease Characteristics

Pooled ADvocate1&2	LEBRI 250 mg Q2W (N=564)
Age, years	36.4 (17.3)
Adolescent (≥12 to <18), n (%)	67 (11.9)
Adult (≥18), n (%)	497 (88.1)
Male, n (%)	287 (50.9)
Race, n (%)	
White	364 (64.5)
Asian	117 (20.7)
Black	58 (10.3)
Other	25 (4.4)
Duration since AD diagnosis, years	21.4 (15.0)
IGA, n (%)	
3 (Moderate)	345 (61.2)
4 (Severe)	219 (38.8)
EASI	29.3 (11.6)
BSA % involvement	45.7 (22.5)
Pruritus NRS	7.2 (1.9)
<4, n (%)	30 (5.5)
≥4, n (%)	516 (94.5)

Data are mean (SD) unless stated otherwise

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1. Grant L, et al. *Dermatitis*. 2019;30:247-254. 2. Okragly AJ, et al. *Dermatol Ther (Heidelb)*. 2023;13:1535-1547. 3. Blauvelt A, et al. *Br J Dermatol*. 2023;188:740-748. 4. Silverberg JI, et al. *N Engl J Med*. 2023;388:1080-1091. 5. Revolutionizing Atopic Dermatitis, 11-13 December 2021. *Br J Dermatol*. 2022;186:e135-185.

ABBREVIATIONS

AD=atopic dermatitis; BSA=body surface area; EASI=Eczema Area and Severity Index; EASI 50/75/90=at least 50/75/90% improvement from baseline in EASI; EMA=European Medicines Agency; FDA=US Food and Drug Administration; IGA=Investigator's Global Assessment; IL=interleukin; IR=inadequate responder; LD=loading dose; LEBRI=lebrikizumab; LTE=long-term extension; MEP=Maintenance Escape Period; MPP=Maintenance Primary Population; MI=multiple imputation; mITT=modified Intent-to-Treat; NRI=non-responder imputation; NRS=Numeric Rating Scale; PBO=placebo; Q2W=every 2 weeks; Q4W=every 4 weeks; SD=standard deviation; W=Week

DISCLOSURES

A. Armstrong has served as a consultant, speaker, and/or investigator for: AbbVie, Almirall, Arcutis, ASLAN Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Dermira, Eli Lilly and Company, EPI Health, Incyte Corporation, Janssen, LEO Pharma, Modernizing Medicine, Nimbus Therapeutics, Novartis, Ortho Dermatologics, PAREXEL, Pfizer, Regeneron, Sanofi Genzyme, SUN Pharma, and UCB Pharma; **K. Ghoreschi** has received honoraria as a consultant, advisory board member, speaker, and/or served as investigator for: AbbVie, Almirall, Boehringer Ingelheim, Bristol Myers Squibb, Eli Lilly and Company, Janssen-Cilag, LEO Pharma, Novartis, Pfizer, and UCB Pharma; **D. Rosmarin** has received honoraria as a consultant, received research support, and/or served as a speaker for: AbbVie, Abcuro, AltruBio, Amgen, Arena Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Concert Pharmaceuticals, CSL Behring, Dermavant, Dermira, Eli Lilly and Company, Galderma, Incyte Corporation, Janssen, Kyowa Kirin, Merck, Novartis, Pfizer, Regeneron, Sanofi, SUN Pharma, UCB Pharma, and Viela Bio; **T. Schlesinger** is a speaker, consultant, and/or investigator for: AbbVie, Almirall, Arcutis, Benev, Bristol Myers Squibb, Crown Aesthetics, Eli Lilly and Company, Genentech, Janssen, LEO Pharma, Pfizer, Regeneron, SUN Pharma, and UCB Pharma, and has served as an Investigator for: Allergan, Arcutis, ASLAN Pharmaceuticals, Biofrontera, Boehringer Ingelheim, Cara Therapeutics, Castle Biosciences, ChemoCentryx, Coherus Biosciences, Concentrics, Concert Pharmaceuticals, Cutanea, Dermavant, Dermira, Eli Lilly and Company, Galderma, Incyte Corporation, Janssen, Nimbus Therapeutics, Novartis, Processa, Prolacta, Regeneron, Sanofi, and Trevi Pharmaceuticals, and is a shareholder of: Bristol Myers Squibb, Eli Lilly and Company, Greenway Therapeutix, and Remedy, and is a consultant for: RBC Consultants; **A. Irvine** is a consultant and/or advisory board member and/or is on the Data Safety Monitoring Board for: AbbVie, Arena Pharmaceuticals, BenevolentAI, Eli Lilly and Company, LEO Pharma, Novartis, Pfizer, Regeneron, and Sanofi, has received research grants from: AbbVie and Pfizer; is on the board of directors of: the International Eczema Council; provides research support to: Regeneron; and is on the speaker's bureau for: AbbVie, Eli Lilly and Company, Regeneron, and Sanofi Genzyme; **A. Bewley** has received honoraria and/or consulting fees from: AbbVie, Almirall, Eli Lilly and Company, Galderma, Janssen, LEO Pharma, Novartis, Sanofi, and UCB Pharma and is a board member of: British Association of Dermatologists, European Society for Dermatology and Psychiatry, Ichthyosis Support Group, National Eczema Society, and Psoriasis Association; **M. Casillas**, **G. Gallo**, **Y. Ding**, and **C. Xu** are employees and shareholders of: Eli Lilly and Company; **I. Pau-Charles** is a current employee and shareholder of: Almirall, **E. Simpson** reports personal fees from: AbbVie, Advances in Cosmetic Medical Derm Hawaii, Amgen, AOBiome, Arcutis Biotherapeutics, Arena Pharmaceuticals, Aslan Pharma, Boehringer Ingelheim, Boston Consulting Group, Bristol Myers Squibb, Collective Acumen, CorEvitas, Dermira, Eli Lilly and Company, Evelo Biosciences, Evidera, Excerpta Medica, FIDE, Forte Bio RX, Galderma, GlaxoSmithKline, Gilead Sciences, Incyte Corporation, Innovaderm Reche, Janssen, Johnson & Johnson, Kyowa Kirin, LEO Pharma, Medscape, Merck, MauiDerm, MLG Operating, MJH holding, Pfizer, Physicians World, PRIME, Recludix Pharma, Regeneron, Revolutionizing Atopic Dermatitis, Roivant, Sanofi Genzyme, Trevi Therapeutics, Valeant, Vindico Medical Education, and WebMD, and has received grants (or serves as Principal investigator role) from: AbbVie, Acrotech Biopharma Inc, Amgen, Arcutis, ASLAN Pharmaceuticals, Castle Biosciences, CorEvitas, Dermavant, Dermira, Eli Lilly and Company, Incyte Corporation, Kymab, Kyowa Kirin, National Jewish Health, LEO Pharma, Pfizer, Regeneron, Sanofi, and Target RWE

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